REMARKS

Claims 14, 21, 22, 23, 24, 25, 26, 27, 28, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48 and 49 are pending in the instant application.

Claims 14, 21, 22, 23, 24, 25, 26, 27, 28, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48 and 49 are rejected.

Claims 14, 24, 28, 38, 39, 40, 44, 45 and 46 have been amended. Support for this amendment is provided in the specification at page 3, lines 26-29 and page 7, lines 2-5. Thus no new matter is added by this amendment.

Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph

Claims 14, 21, 22, 23, 24, 25, 26, 27, 28, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48 and 49 stand rejected under 35 U.S.C. 101 because the Examiner suggests that the claimed invention is not supported by either a substantial asserted utility or a well established utility. In particular, the Examiner suggests that the specification

did not teach the protein sequence or the open reading frame of SEQ ID NO:1 and therefore did not provide enough information to indicate for which protein the claimed antibody is specific. Further, the Examiner suggests that the specification does not describe a utility for an antibody with unknown specificity and one of skill would doubt any truth to a stated utility.

Claims 14, 21, 22, 23, 24, 25, 26, 27, 28, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48 and 49 also stand rejected under 35 U.S.C. 112, first paragraph, because the Examiner suggests that without support of a substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed invention.

Applicants respectfully traverse these rejections.

To meet the utility requirements of 35 U.S.C. 101 and use requirements of 35 U.S.C. 112, first paragraph, the utility of the invention must be well-established or the specification must set forth a substantial utility for the claimed invention.

Claims of the instant application have been amended herein to state that the antibody or antibody fragment

binds specifically to **native** protein encoded by polynucleotide sequence SEQ ID NO:1 or to a fragment of native protein encoded by polynucleotide sequence SEQ ID NO:1, wherein the fragment of the native protein encoded by polynucleotide sequence SEQ ID NO:1 is encoded by polynucleotide sequence SEQ ID NO:12 or 13; and methods for binding these antibodies or antibody fragments on a cell by contacting the cell with the isolated antibody or antibody fragment. Support for this amendment is provided in the specification at page 3, lines 26-29 and page 7, lines 2-5.

Utility of the claimed antibodies is taught in the specification.

Specifically, at page 3, line 26 through page 4, line 2, as well as page 7, lines 2-35, of the specification, it is taught that nine Cancer Specific Genes (CSGs) have been identified and refer, among other things, to native proteins expressed by the genes comprising the polynucleotide sequences of any of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8 or 9, the native mRNAs encoded by the genes comprising any of the polynucleotide sequences of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8 or 9 or the actual genes comprising any of the polynucleotide sequences of SEQ ID

NO: 1, 2, 3, 4, 5, 6, 7, 8 or 9. It is also taught that fragments of the CSGs such as those characterized by SEQ ID NO:10, 11, 12, 13 or 14 can also be detected.

Further, at page 6, lines 3 through 20, of the specification it is stated that:

> antibodies against CSG or fragments of such antibodies which can be used to detect or image localization of CSG in a patient for the purpose of detecting or diagnosing selected cancers. Such antibodies can be polyclonal or monoclonal, or prepared by molecular biology techniques. The term "antibody", as used herein and throughout the instant specification is also meant to include aptamers and single-stranded oligonucleotides such as those derived from an *in vitro* evolution protocol referred to as SELEX and well known to those skilled in the art. Antibodies can be labeled with a variety of detectable labels including, but not limited to, radioisotopes and paramagnetic metals. These antibodies or fragments thereof can also be used as therapeutic agents in the treatment of diseases characterized by expression of a CSG. In therapeutic applications, the antibody can be used without or with derivatization to a cytotoxic agent such as a radioisotope, enzyme, toxin, drug or a prodrug.

Further, at page 11, line 5 through page 12, line 7 of the instant specification, assay techniques that can be used to determine levels of a CSG of the present invention, in a sample derived from a patient are described. Included in the assays taught in the specification are radioimmunoassays, immunohistochemistry assays, competition

assays, Western Blot analyses and ELISA assays, all of which are well known to those of skill in the art and involve antibodies to the CSG. ELISA and competition assays are described in detail at page 11, line 16 through page 12, line 7 and page 12, lines 8 through 29, respectively, and each assays is explicitly stated to require an antibody specific to CSG.

In addition, in vivo antibody uses are taught in the specification at page 14, line 5 through page 15, line 27 in a subsection of the specification entitled ***"In Vivo Antibody Use"***. Therein it is stated that:

> Antibodies against CSG can also be used *in vivo* in patients suspected of suffering from a selected cancer including lung cancer or gynecologic cancers such as ovarian, breast, endometrial or uterine cancer [and that] antibodies against a CSG can be injected into a patient suspected of having a selected cancer for diagnostic and/or therapeutic purposes.

It is further stated that "use of antibodies for *in vivo* diagnosis is well known in the art" and several examples of antibodies used as in vivo diagnostics in cancer are provided in the specification as evidence to support this statement. In addition, details on administering antibodies against a CSG for the purpose of diagnosing or staging of the disease status of the patient are set forth

as well as injection of an antibody against a CSG for therapeutic benefit. Again, several examples of antibodies used as therapeutics in cancer are provided in the specification. These examples are evidence of the credibility of substantial asserted utility of the instant claimed invention.

Thus, teachings of the original, as-filed specification clearly assert a substantial utility for the claimed invention.

Further, the case law if clear - compliance with 35 U.S.C. 101 is a question of fact. Raytheon v. Roper, 724 F.2d 951,956, 220 USPQ 592, 596 (Fed. Cir. 1983, cert denied, 469 U.S. 835 (1984). To overcome the presumption of truth that an assertion of utility by the applicant enjoys, Office personnel must establish that it is more likely than not that one or ordinary skill in the art would doubt (i.e. "question") the truth of the statement of utility. To do this, Office personnel must provide **evidence** sufficient to show that the statement of asserted utility would be considered "false" by a person of ordinary skill in the art. MPEP 2107.02.

The Examiner states in the July 28, 2006 Office Action that one of ordinary skill in the art would doubt any truth to a stated utility of the claimed invention. No evidence to support this statement by the Examiner is provided. Instead, the Examiner appears to base this statement upon personal interpretation and opinion that "the specification did not teach the protein sequence or the open reading frame of SEQ ID NO:1" and that "the specification did not provide enough information to indicate for which protein the claimed antibody is specific for".

Applicants respectfully disagree.

Express teachings in the specification of native protein encoded by SEQ ID NO:1 is not required to meet the requirements of 35 U.S.C. 101 and 35 U.S.C. 112.

Instead, MPEP 2107.01 is clear; to satisfy the requirements of 35 U.S.C. 101, an applicant must claim an invention that is statutory subject matter and must show that the claimed invention is useful for some purpose either expressly **or implicitly** (emphasis added).

The sequence of native protein encoded by SEQ ID NO:1 is clearly implicit in teachings of specification, and therefore is supported by the stated utilities discussed

supra. This is especially clear in light of the general knowledge in the art, as evidenced by publications available as of the filing date, for identifying the open reading frame of a polynucleotide sequence such as SEQ ID NO:1 and software tools to automate this routine practice.

General knowledge in the art known as of the filing date of the instant application included that the sequence flanking a functional protein transcription initiator codon in a eukaryotic mRNA sequence is a nonrandom sequence, referred to as the Kozak consensus sequence (see Kozak, M. Nucleic Acids Research 1981 9(20):52335262; Kozak, M. Nucleic Acids Research 1984 12(2):857-872; and Kozak, M. Nucleic Acids Research 1987 15(20):8125-8148). Further, it was known from multiple references (e.g., Kozak, M. Nucleic Acids Research 1984 12(2):857-872, Singer, M. and Berg, P. Genes & Genomes 1991 University Science Books (Mill Valley, CA), pages 180-182; and Watson et al. Molecular Biology of the Gene 1987 The Benjamin/Cummings Publishing Company, Inc. (Menlo Park, CA)) that the 5'-proximal ATG serves as the initiator codon for the majority of mRNAs.

As discussed in detail in paragraph 6 of Dr. Salceda's Declaration, protein sequences and/or open reading frames

for polynucleotides were routinely obtained by those skilled in the art at the time of filing the instant patent application based upon information such as provided in the instant specification. In particular, the specification teaches in Examples 1 and 2 that SEQ ID NO:1 is an mRNA molecule and thus has a set 5' to 3' orientation. See in particular pages 16-18 of the instant specification. From this information, Dr. Salceda advised that one skilled in the art would know that the protein is encoded in the forward (5' to 3') direction of SEQ ID NO:1. See paragraph 6 of Dr. Salceda's Declaration. As also made clear in paragraph 6 of Dr. Salceda's Declaration, multiple tools were available by 1998, thus preceding the September 2, 1998 priority date of the instant application, which could be used to routinely determine the protein sequence and/or open reading frame of SEQ ID NO:1 based upon the information provided in the instant specification in an expedited fashion. Examples of results from three different computer programs available to those skilled in the art as of the filing date of the instant application were provided with Dr. Salceda's Declaration.

Accordingly, based upon teachings in the specification of polynucleotide SEQ ID NO:1, its 5' to 3' orientation and what was well known as of the filing date of the instant application, one of skill in the art would know that for the polynucleotide SEQ ID NO:1, there was only one possible frame to encode native protein, frame 2.

Finally, MPEP 2107.02B teaches where an applicant has specifically asserted that an invention has a particular utility, the assertion cannot simply be dismissed by Office personnel as being "wrong" even when there may be reason to believe that the assertion is not entirely accurate. Rather, Office personnel must determine if the assertion of utility is credible (i.e. whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) facts upon which the assertion is based are inconsistent with the logic underlying the assertion.

For the instant invention, the logic underlying the asserted utility is clearly not flawed. Nor are the facts

upon which the assertion is based inconsistent with the logic underlying the assertion.

Instead, the asserted utility has been confirmed in publications by Tringler et al. and Salceda et al. (previously submitted).

Accordingly, the record as a whole makes it more likely than not that the asserted utility for the claimed invention would be considered credible by a person of ordinary skill in the art. Thus, the Office cannot maintain this utility rejection. In re Rinehart 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976).

Withdrawal of these rejections under 35 U.S.C. 101 and 35 U.S.C. 112, is therefore respectfully requested.

II. Rejection of Claims under 35 U.S.C. 112, first paragraph - written description

Claims 14, 21, 22, 23, 24, 25, 26, 27, 28, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48 and 49 have been rejected of 35 U.S.C. 112, first paragraph for failing to meet the written description requirement. The Examiner suggests that Applicants were not in possession of any

protein encoded by SEQ ID NO:1, or just any fragments of SEQ ID NO:1, 10-13 or 16.

Applicants respectfully traverse this rejection.

At the outset, it is respectfully pointed out that the claims of the instant application have been amended herein to state that the antibody or antibody fragment binds specifically to **native** protein encoded by polynucleotide sequence SEQ ID NO:1 or to a fragment of native protein encoded by polynucleotide sequence SEQ ID NO:1, wherein the fragment of the native protein encoded by polynucleotide sequence SEQ ID NO:1 is encoded by polynucleotide sequence SEQ ID NO:12 or 13; and methods for binding these antibodies or antibody fragments on a cell by contacting the cell with the isolated antibody or antibody fragment. Support for this amendment is provided in the specification at page 3, lines 26-29 and page 7, lines 2-5.

Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and

knowledge in the art, partial structure and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. See MPEP 2163 at page 2100-73 and Regents of the University of California v. Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406 (Fed. Cir. 1997).

Precisely how close [to the claimed invention] the description must come to comply with § 112 must be left to case-by-case-development. In re Wertheim, 541 F.2d at 262, 191 USPQ at 96 (inquiry is primarily factual and depends on the nature of the invention and the amount of the knowledge imparted to those skilled in the art by the disclosure).

In the instant case, Applicants provided in the originally filed specification the nucleic acid sequences for polynucleotide SEQ ID NO:1, and multiple fragments thereof including SEQ ID NO:12 and 13. Further, Applicants

have taught in the originally filed specification that SEQ ID NO:1 is an mRNA, thus establishing its 5' to 3' orientation. Polynucleotide SEQ ID NO:1 is inclusive of the entire open reading frame for the native protein encoded thereby. The polynucleotide SEQ ID NO:1 has a protein translation initiation codon sequences, a characteristic known as a Kozak consensus sequence. The Kozak consensus sequence is well established in the art as a non-random sequence flanking functional initiator codons where protein translation begins in the majority of eukaryotic mRNA sequences (see Kozak, M. Nucleic Acids Research 1981 9(20):52335262; Kozak, M. Nucleic Acids Research 1984 12(2):857-872; and Kozak, M. Nucleic Acids Research 1987 15(20):8125-8148). Further, this Kozak consensus sequence flanks the 5'-proximal ATG, well known in the art to serve as the initiator codon for the majority of mRNAs.

Thus, the nucleic acid sequence taught for polynucleotide SEQ ID NO:1 in the originally filed specification includes the classic structural characteristics well established in the art which define

the open reading frame of a nucleic acid sequence which encodes the native protein.

Further, as already outlined in detail in Section I of this response, the instant application includes a description of various methods for making the claimed antibodies and methods for using the antibodies.

Thus, for this case, wherein:

(1) the claims are drawn to an isolated antibody or antibody fragment that bind specifically to native protein encoded by polynucleotide sequence SEQ ID NO:1; and

(2) the disclosure teaches multiple structural characteristics for polynucleotide SEQ ID NO:1 defining the native protein encoded thereby as well as detailed teachings for production and use of an antibody to native protein encoded thereby;

the disclosure distinguishes the claimed invention from other materials and makes clear to one of skill in the art that Applicants were in possession of the claimed species.

The case law is clear; as long as the skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, every nuance

of the claims need not be explicitly described in the specification to meet the written description. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991).

Accordingly, any requirement for an explicit description in the specification of the amino acid sequence of the native protein encoded by SEQ ID NO:1 to meet the written description requirement, when the disclosed structural characteristics of polynucleotide SEQ ID NO:1 coupled with detailed teachings of methods for production and use of the claimed antibodies is unwarranted.

Also clear in the case law, is that in most technologies which are mature, wherein the knowledge and level of skill in the art is high, a written description question should not be raised for original claims even if the specification discloses only a method of making the invention and the function of the invention. See, e.g. In re Hayes Microcomputer Products, Inc. Patent Litigation, 982 F.2d 1527, 1534-1535, 25 USPQ2d 1241, 1246 (Fed. Cir. 1992). The patents and printed publications in this art, which are to be relied upon to determine maturity and level of knowledge, clearly demonstrate protein and antibody

production to be a mature art with a high level of knowledge and skill is in the art. Applicants have provided multiple references published prior to the filing date of the instant application during the prosecution of this case evidencing a very high level of skill in the art of characterizing encoded proteins. Further, the polynucleotide SEQ ID NO:1 contains the defined structural characteristics those skilled in the art routinely use to identify the open reading frame and protein encoded by a polynucleotide such as SEQ ID NO:1. In addition, the Declaration by Dr. Susana Salceda, makes clear that while every nuance of the protein sequence and/or open reading frame of SEQ ID NO:1 may not have been explicitly described in the specification, sufficient distinguishing characteristics were taught in the specification so that using standard knowledge of those skilled in the art as of the filing date of the instant application this information could be routinely determined.

Thus, for this case, wherein the original claims were drawn to antibodies and the specification discloses a method of making the claimed invention and the function of

the invention, a written description question should not be raised.

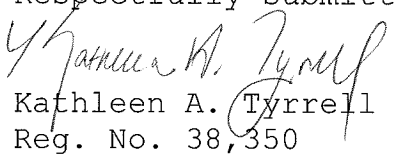
Finally, MPEP 2163 at page 2100-169, col. 2, states that the "absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. 112, paragraph 1, for lack of written description." The evidence presented by Applicant during prosecution of this case clearly demonstrates that characterization of the coding region of polynucleotide SEQ ID NO:1 and the encoded native protein could be routinely determined based upon the structural characteristics taught in the instant application coupled with well-established procedures. Accordingly, absence of details of this coding region or the encoded protein in the instant specification should not be the basis of a rejection under 35 U.S.C. 112, first paragraph, for lack of written description.

Withdrawal of this rejection under 35 U.S.C. 112, first paragraph, for lack of written description is respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



Kathleen A. Tyrrell
Reg. No. 38,350

Date: **March 28, 2007**

LICATA & TYRRELL P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515